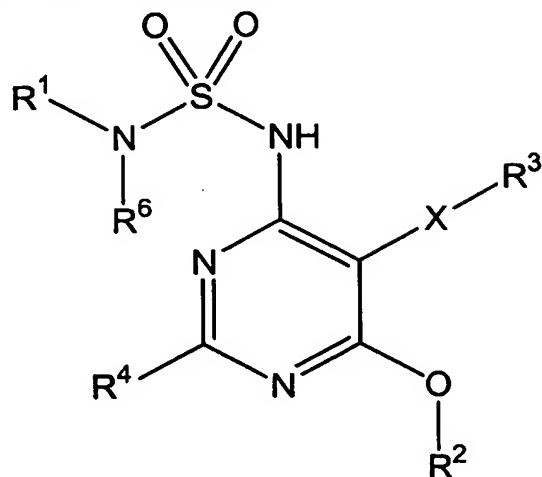


Claims

1. Compounds of the **general formula I**,



General Formula I

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wherein

R¹ represents lower alkyl-O-(CH₂)_n-, cycloalkyl-O-(CH₂)_n-,
cycloalkyl-CH₂-O-(CH₂)_n-;

10 **R²** represents -CH₃; R^a-Y-(CH₂)_m-;

R³ represents aryl; heteroaryl;

15 **R⁴** represents hydrogen; trifluoromethyl; lower alkyl; lower alkyl-amino; lower alkyloxy; lower alkyloxy-lower alkyloxy; hydroxy-lower alkyloxy; lower alkyl-sulfinyl; lower alkylthio; lower alkylthio-lower alkyl; hydroxy-lower alkyl; lower alkyloxy-lower alkyl; hydroxy-lower alkyloxy-lower alkyl; hydroxy-lower alkyl-amino; lower alkylamino-lower alkyl; amino; di-lower alkylamino; [N-(hydroxy-lower alkyl)-N-(lower alkyl)]-amino; aryl; arylamino; aryl-lower alkylamino; aryl-thio; aryl-lower alkylthio; aryloxy; aryl-lower alkyloxy; aryl-lower alkyl; arylsulfinyl; 20 heteroaryl; heteroaryl-oxy; heteroaryl-amino; heteroarylthio; heteroaryl-lower alkyl; heteroarylsulfinyl; heterocyclyl; heterocyclyl-lower alkyloxy; heterocyclyoxy; heterocyclylamino; heterocyclyl-lower alkylamino; heterocyclylthio; heterocyclyl-lower alkylthio; heterocyclyl-lower alkyl; heterocyclylsulfinyl; cycloalkyl;

cycloalkyloxy; cycloalkyl-lower alkyloxy; cycloalkylamino; cycloalkyl-lower alkylamino; cycloalkylthio; cycloalkyl-lower alkylthio; cycloalkyl-lower alkyl; cycloalkylsulfinyl;

5 R^6 represents hydrogen or methyl;

X represents oxygen; sulfur; $-CH_2-$ or a bond;

Y represents a bond, $-O-$; $-NH-$; $-SO_2-NH-$; $-NH-SO_2-NH-$; $-O-CO-$; $-CO-O-$;
10 $-O-CO-NH-$; $-NH-CO-O-$; $-NH-CO-NH-$;

n represents the integers 2, 3, or 4;

m represents the integers 2, 3, or 4;

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R^a represents aryl, heteroaryl, lower alkyl, cycloalkyl, hydrogen;

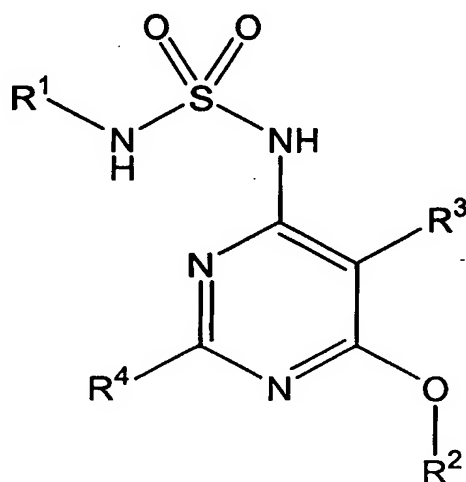
and optically pure enantiomers, mixtures of enantiomers such as for example
20 racemates, optically pure diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates and the meso-forms and pharmaceutically acceptable salts thereof.

2. Compounds of general formula I in claim 1, wherein R^1 , R^2 , R^4 and R^6 are as
25 defined in general formula I in claim 1, R^3 represents phenyl, mono- or di-substituted phenyl substituted with ethoxy, methoxy or chlorine and X represents oxygen, and pharmaceutically acceptable salts thereof.

3. Compounds of general formula I in claim 1, wherein R^1 , R^4 and R^6 are as
30 defined in general formula I in claim 1, R^3 represents phenyl, mono- or di-substituted phenyl substituted with ethoxy, methoxy or chlorine, X represents oxygen and R^2 represents $-(CH_2)_m-Y-R^a$, and pharmaceutically acceptable salts thereof.

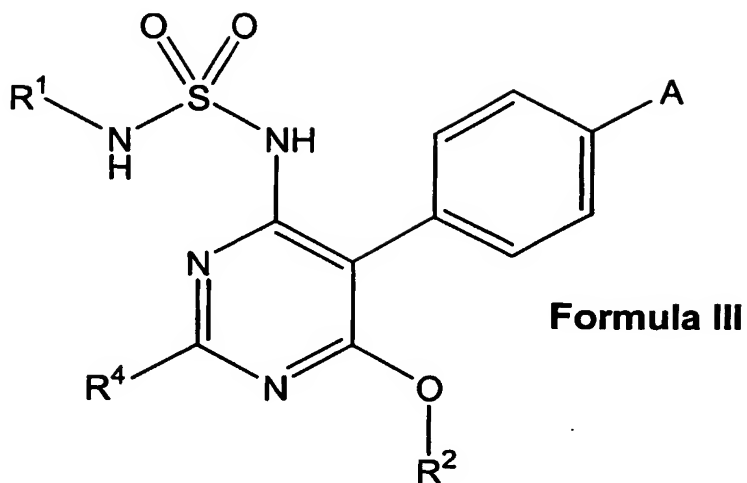
4. Compounds of general formula I in claim 1, wherein R^1 , R^4 and R^6 are as defined in general formula I in claim 1, R^3 represents phenyl, mono- or di-substituted phenyl substituted with ethoxy, methoxy or chlorine, X represents oxygen and R^2 represents $-(CH_2)_2-O-R^a$, with R^a being heteroaryl, and pharmaceutically acceptable salts thereof.

5. Compounds of formula II

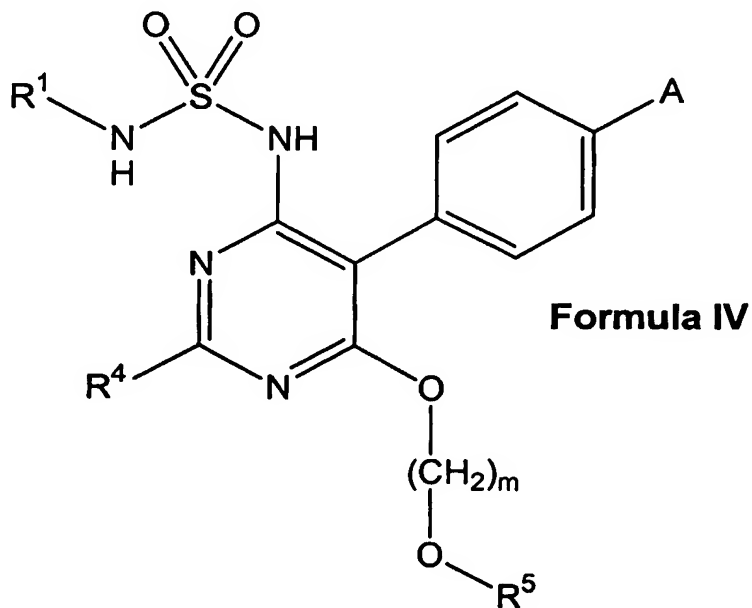


Formula II

wherein R^1 , R^2 , R^3 and R^4 are as defined in general formula I in claim 1, and pharmaceutically acceptable salts of compounds of formula II.

6. Compounds of **formula III**

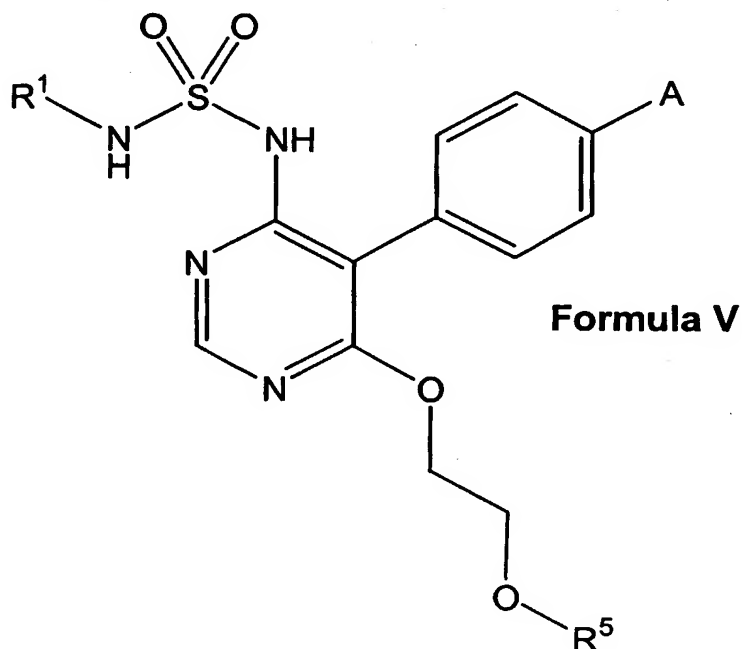
- 5 wherein R^1 , R^2 and R^4 are as defined in general formula I in claim 1 and A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy, and pharmaceutically acceptable salts of compounds of formula III.

10 7. Compounds of **formula IV**

wherein R^1 , R^4 and m are as defined in general formula I in claim 1, A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy, and R^5 represents aryl or heteroaryl, and pharmaceutically acceptable salts of compounds of formula IV.

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8. Compounds of formula V



wherein R^1 is as defined in general formula I in claim 1, A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy and R^5 represents aryl or heteroaryl, and pharmaceutically acceptable salts of compounds of formula V.

9. Compounds of formula V wherein R^1 is as defined in general formula I in claim 1, A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy and R^5 represents a substituted pyrimidine, and pharmaceutically acceptable salts of compounds of formula V.

10. Compounds of general formula I in claim 1, wherein R^1 represents $CH_3O-CH_2CH_2-$, R^6 represents hydrogen and R^2 , R^3 , and R^4 are as defined in general formula I in claim 1, and pharmaceutically acceptable salts of compounds thereof.

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11. Compounds of formula V in claim 8, wherein R^1 represents $CH_3-O-CH_2CH_2-$, A represents hydrogen, methyl, ethyl, chlorine, bromine, fluorine, trifluoromethyl or methoxy and R^5 represents aryl or heteroaryl, and pharmaceutically acceptable salts of compounds of formula V in claim 8.

12. Compounds selected from the group consisting of:

2-Methoxy-ethanesulfamic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-chloro-5-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

2-Methoxy-ethanesulfamic acid {5-(4-bromophenyl)-6-[2-(5-bromopyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide;

2-Methoxy-ethanesulfamic acid {5-(4-bromophenyl)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide;

2-Methoxy-ethanesulfamic acid {5-(4-bromophenyl)-6-[2-(5-methoxypyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide.

13. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of disorders which are associated with a role of endothelin.

14. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of circulatory disorders which are associated with a role of endothelin.

15. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of inflammatory disorders which are associated with a role of endothelin.

16. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of proliferative disorders which are associated with a role of endothelin.

17. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine,

subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, complications of vascular or cardiac surgery or after organ transplantation, and complications of cyclosporin, the therapy and prophylaxis of diabetic complications.

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18. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of disorders which are associated with a role of endothelin, and require mixed ET_A and ET_B blocking for treatment.

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19. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of disorders which are associated with a role of endothelin, and require selective ET_A blocking for treatment.

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20. Compounds of any one of the claims 1 to 12 for use as medicaments for the treatment of disorders which are associated with a role of endothelin, and require selective ET_B blocking for treatment.

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21. The use of one or more compounds of any one of claims 1 to 12 as active ingredients for the production of pharmaceutical compositions for the treatment of disorders associated with a role of endothelin.

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22. The use of one or more compounds of any one of claims 1 to 12 as active ingredients for the production of pharmaceutical compositions for the treatment of circulatory disorders which are associated with a role of endothelin.

23. The use of one or more compounds of any one of claims 1 to 12 as active ingredients for the production of pharmaceutical compositions for the treatment of inflammatory disorders which are associated with a role of endothelin.

24. The use of one or more compounds of any one of claims 1 to 12 as active ingredients for the production of pharmaceutical compositions for the treatment of proliferative disorders which are associated with a role of endothelin.

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25. The use of one or more compounds of any one of claims 1 to 12 as active ingredients for the production of pharmaceutical compositions for the treatment of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine, subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, melanoma, prostatic cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, therapy and prophylaxis of diabetic complications, complications of vascular or cardiac surgery or after organ transplantation, and complications of cyclosporin.

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26. The use of one or more compounds of any one of claims 1 to 12 as active ingredients in combination with one or more other substances therapeutically useful for the treatment of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine, subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, melanoma, prostatic cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, therapy and prophylaxis of diabetic complications, complications of vascular or cardiac surgery or after organ transplantation, and complications of cyclosporin.

27. A process for the manufacture of pharmaceutical compositions for the treatment of disorders associated with a role of endothelin containing one or more compounds as claimed in any one of claims 1 to 12 as active ingredients which process comprises mixing one or more active ingredients with pharmaceutically
5 acceptable excipients in a manner known per se.